

RESPONSE TO ELECTION OF
SPECIES REQUIREMENT
U.S. Appln. No. 09/674,377

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS

Claim 1. (Currently Amended) A neovascularization inhibitor comprising the following polypeptide (a) or (b) as an active ingredient:

- (a) a polypeptide having the amino acid sequence PyrGlu³² ~ Val⁴⁷⁸ of hepatocyte growth factor-; or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence of (a) by the deletion, substitution or addition of one or more amino acids and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF.

Claim 2. (Currently Amended) A neovascularization inhibitor comprising the following polypeptide (a) or (b) as an active ingredient:

- (a) a polypeptide having the amino acid sequence PyrGlu³² ~ Val⁴⁷⁸ of hepatocyte growth factor (HGF)-; or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or more amino acids, and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF and inhibitory action against the

**RESPONSE TO ELECTION OF
SPECIES REQUIREMENT
U.S. Appln. No. 09/674,377**

growth of vascular endothelial cells induced by
bFGF and/or VEGF.

Claim 3. (Currently Amended) A neovascularization inhibitor as set forth in ~~paragraph~~claim 1 or 2, wherein said polypeptide has at least one hairpin domain and 4 Kringle domains.

Claim 4. (Currently Amended) A neovascularization inhibitor as set forth in ~~paragraph~~claim 1 or 2, wherein said polypeptide is one obtainable by elastase digestion of hepatocyte growth factor.

Claim 5. (Original) A neovascularization inhibitor comprising the polypeptide defined by SEQ ID NO:1 and a pharmaceutically acceptable carrier.

Claim 6. (Original) A neovascularization inhibitor comprising the polypeptide defined by SEQ ID NO:2 and a pharmaceutically acceptable carrier.

Claim 7. (Currently Amended) A prophylactic or therapeutic drug for a disease associated with abnormal angiopoiesis which comprises the polypeptide as set forth in ~~paragraph~~claim 1 or 2, and a pharmaceutically acceptable carrier.

Claim 8. (Currently Amended) A prophylactic or therapeutic drug as set forth in ~~paragraph~~claim 7, wherein said disease associated with abnormal angiopoiesis is selected from the group consisting of rheumatoid arthritis, psoriasis, Osler-Webber syndrome, myocardial angiopoiesis, telangiectasia, hemophilic joint, angiogenic diseases of the eye, angiofibroma, benign tumors and wound granulation.

RESPONSE TO ELECTION OF
SPECIES REQUIREMENT
U.S. Appln. No. 09/674,377

Claim 9. (Currently Amended) A prophylactic or therapeutic drug for a disease arising from overstimulation of endothelial cells which comprises the polypeptide as set forth in ~~paragraph~~ claim 1 or 2, and a pharmaceutically acceptable carrier.

Claim 10. (Currently Amended) A prophylactic or therapeutic drug as set forth in ~~paragraph~~ claim 9, wherein said disease arising from overstimulation of endothelial cells is selected from the group consisting of enteric adhesion, Crohn's disease, atherosclerosis, scleroderma and overcicatrization.

Claim 11. (Currently Amended) A conception-regulating drug comprising the polypeptide as set forth in ~~paragraph~~ claim 1 or 2, and a pharmaceutically acceptable carrier.

Claim 12. (Currently Amended) A method of inhibiting neovascularization which comprises administering to a subject a neovascularization inhibitor comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

(a) a polypeptide having the amino acid sequence
PyrGlu³² ~ Val⁴⁷⁸ of hepatocyte growth factor
(HGF~~+~~); or

(b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or more amino acids and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF.

Claim 13. (Currently Amended) A method of inhibiting neovascularization which comprises administering to a subject a

RESPONSE TO ELECTION OF
SPECIES REQUIREMENT
U.S. Appln. No. 09/674,377

neovascularization inhibitor comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

- (a) a polypeptide having the amino acid sequence PyrGlu³² ~ Val⁴⁷⁸ of hepatocyte growth factor (HGF~~+-~~); or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or more amino acids, and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF and inhibitory action against the growth of vascular endothelial cells induced by bFGF and/or VEGF.

Claim 14. (Currently Amended) A method for prophylaxis or therapy of a disease associated with abnormal angiopoiesis which comprises administering a neovascularization inhibitor comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

- (a) a polypeptide having the amino acid sequence PyrGlu³² ~ Val⁴⁷⁸ of hepatocyte growth factor (HGF~~+-~~); or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or more amino acids and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF to a subject in whom a prophylactic

RESPONSE TO ELECTION OF
SPECIES REQUIREMENT
U.S. Appln. No. 09/674,377

or therapeutic treatment for said disease is indicated.

Claim 15. (Currently Amended) A method for prophylaxis or therapy of a disease associated with abnormal angiogenesis which comprises administering a neovascularization inhibitor comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

- (a) a polypeptide having the amino acid sequence PyrGlu³² ~ Val⁴⁷⁸ of hepatocyte growth factor (HGF~~+-~~); or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or more amino acids, and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF and inhibitory action against the growth of vascular endothelial cells induced by bFGF and/or VEGF to a subject in whom a prophylactic or therapeutic treatment for said disease is indicated.

Claim 16. (Currently Amended) The method for prophylaxis or therapy as set forth in ~~paragraph~~ claim 14 or 15, wherein said disease is any disease selected from the group consisting of rheumatoid arthritis, psoriasis, Osler-Webber syndrome, myocardial angiogenesis, telangiectasia, hemophilic joint, angiogenic diseases of the eye, angiofibroma, benign tumors, wound granulation, enteric adhesion, Crohn's disease, atherosclerosis, scleroderma and overcicatrizization.

**RESPONSE TO ELECTION OF
SPECIES REQUIREMENT
U.S. Appln. No. 09/674,377**

Claims 17-18. (Cancelled)

Claim 19. (Previously Presented) A polypeptide having an amino acid sequence defined by SEQ ID NO:2.

Claim 20. (Previously Presented) A pharmaceutical composition containing the polypeptide having an amino acid sequence defined by SEQ ID NO:2 as an active ingredient.

Claim 21. (Previously Presented) A pharmaceutical composition for prophylaxis or therapy of a solid cancer or/and cancer metastasis, which comprises the polypeptide having an amino acid sequence defined by SEQ ID NO:2 as an active ingredient.

Claim 22. (Previously Presented) A pharmaceutical composition as claimed in Claim 21, wherein cancer of solid cancer or cancer of cancer metastasis is lung cancer or mammary cancer.

Claim 23. (Previously Presented) A pharmaceutical composition effective for inhibition of tumor growth or metastasis, which comprises the polypeptide having an amino acid sequence defined in SEQ ID NO:2 as an active ingredient.

Claim 24. (Previously Presented) A pharmaceutical composition as claimed in Claim 23, wherein tumor is lung cancer or mammary cancer.

Claim 25. (Previously Presented) A pharmaceutical composition for prophylaxis or therapy of diseases arising from vascular hyperplasia or/and diseases caused by an excessive or abnormal stimulation of the endothelial cells, which comprises the polypeptide having an amino acid sequence defined by SEQ ID NO:2 as an active ingredient.

**RESPONSE TO ELECTION OF
SPECIES REQUIREMENT
U.S. Appln. No. 09/674,377**

Claim 26. (Currently Amended) A pharmaceutical composition as claimed in Claim 25, wherein said disease is a disease selected from the group consisting of rheumatoid arthritis, psoriasis, Osler-Webber syndrome, myocardial angiopoiesis, telangiectasia, hemophilic joint, angiogenic diseases of the ~~eyes~~ eyes, angiofibroma, benign tumors, hematopoietic malignancies, wound granulation, enteric adhesion, Crohn's disease, atherosclerosis, scleroderma and overcicatrizization.

Claim 27. (Previously Presented) A pharmaceutical composition for controlling conception, which comprises the polypeptide having an amino acid sequence defined by SEQ ID NO:2 as an active ingredient.

Claim 28. (Currently Amended) A method for prophylaxis or therapy of a solid cancer and/or cancer metastasis, which comprises administering to a subject a pharmaceutical composition containing the following polypeptide (a) or (b):

- (a) a polypeptide having the amino acid sequence
PyrGlu³²~Val⁴⁷⁸ of heaptocyte growth factor (HGF);
and/or
- (b) a polypeptide having an amino acid sequence
derived from the amino acid sequence defined in
(a) by the deletion, substitution or addition of
one or more amino acids.

Claim 29. (Previously Presented) A method for prophylaxis or therapy of a solid cancer and/or cancer metastasis, which comprises administering to a subject a pharmaceutical composition containing the polypeptide having an amino sequence defined by SEQ ID NO:1 or SEQ ID NO:2.

**RESPONSE TO ELECTION OF
SPECIES REQUIREMENT
U.S. Appln. No. 09/674,377**

Claim 30. (Previously Presented) A method for prophylaxis or therapy as claimed in Claim 28 or Claim 29, wherein cancer of solid cancer or cancer of cancer metastasis is lung cancer or mammary cancer.

Claim 31. (Currently Amended) A method for inhibition of tumor growth or metastasis, which comprises administering to a subject a pharmaceutical composition containing the following polypeptide (a) or (b):

- (a) a polypeptide having the amino acid sequence
PyrGlu³²~Val⁴⁷⁸ of heaptocyte growth factor (HGF);
and/or
- (b) a polypeptide having an amino acid sequence
derived from the amino acid sequence defined in
(a) by the deletion, substitution or addition of
one or more amino acids.

Claim 32. (Previously Presented) A method for inhibition of tumor growth and metastasis, which comprises administering to a subject a pharmaceutical composition containing the polypeptide having an amino acid sequence defined by SEQ ID NO:1 or SEQ ID NO:2.

Claim 33. (Previously Presented) A method for prophylaxis or therapy as claimed in Claim 31 or Claim 32, wherein tumor is lung cancer or mammary cancer.

Claim 34. (Currently Amended) A method for prophylaxis or therapy of diseases arising from vascular hyperplasia and/or diseases caused by an excessive or abnormal stimulation of the endothelial cells, which comprises administering to a subject a

**RESPONSE TO ELECTION OF
SPECIES REQUIREMENT
U.S. Appln. No. 09/674,377**

pharmaceutical composition containing the following polypeptide (a) or (b):

- (a) a polypeptide having the amino acid sequence
PyrGlu³²~Val⁴⁷⁸ of heaptocyte growth factor (HGF);
and/or
- (b) a polypeptide having an amino acid sequence
derived from the amino acid sequence defined in
(a) by the deletion, substitution or addition of
one or more amino acids.

Claim 35. (Previously Presented) A method for prophylaxis or therapy of diseases arising from vascular hyperplasia or/and diseases caused by an excessive or abnormal stimulation of the endothelial cells, which comprises administering to a subject a pharmaceutical composition containing the polypeptide having an amino acid sequence defined by SEQ ID NO:1 or SEQ ID NO:2.

Claim 36. (Currently Amended) A method for prophylaxis or therapy as claimed in Claim 34 or Claim 35, wherein said disease is a disease selected from the group consisting of rheumatoid arthritis, psoriasis, Osler-Webber syndrome, myocardial angiopoiesis, telangiectasia, hemophilic joint, angiogenic diseases of the ~~eyes~~ eyes, angiofibroma, benign tumors, hematopoietic malignancies, wound granulation, enteric adhesion, Crohn's disease, atherosclerosis, scleroderma and overcicatrizization.

Claim 37. (Currently Amended) A method for controlling conception which comprises administering to a subject a

RESPONSE TO ELECTION OF
SPECIES REQUIREMENT
U.S. Appln. No. 09/674,377

pharmaceutical composition containing the following polypeptide

(a) or (b):

(a) a polypeptide having the amino acid sequence
PyrGlu³²~Val⁴⁷⁸ of heaptocyte growth factor (HGF);
and/or

(b) a polypeptide having an amino acid sequence
derived from the amino acid sequence defined in
(a) by the deletion, substitution or addition of
one or more amino acids.